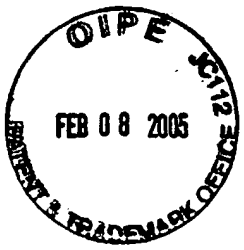

PATENT

ATTORNEY DOCKET NO.: CIT1560-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Benzer and Min	Art Unit:	1614
Application No.:	09/895,141	Examiner	P. G. Spivack
Filed:	June 29, 2001	Confirmation No.:	8276
Title:	LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT		

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL SHEET

Sir:

Transmitted herewith for the above-identified application, please find:

1. Petition Under 37 CFR § 1.181(a) For Withdrawal of Holding of Abandonment (4 pages);
2. Exhibits A through F; and
3. Return Receipt Postcard.

CERTIFICATION UNDER 37 CFR §1.8
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service with sufficient postage as first class mail on this date, February 4, 2005, in an envelope addressed to: MAIL STOP Petitions, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Stephanie Sharrett *(Name of Person Mailing Paper)*
Stephanie Sharrett Feb. 4, 2005 *(Signature)* *(Date)*

GT\6433462.1
104662-101

Applicants do not believe any fees are due in connection with this submission however if any fees are due, the Commissioner is authorized to charge any other fees, or credit any overpayments, to Deposit Account No. 07-1896. A duplicate copy of this Transmittal Sheet is enclosed.

Respectfully submitted,

Date: February 4, 2005

Reg. No. 52,182

0610

Lisa A. Haile, J.D., Ph.D.
Registration No.: 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

USPTO CUSTOMER NUMBER 28213
DLA PIPER RUDNICK GRAY CARY US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133

PATENT
Attorney Docket No.: CIT1560-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Benzer and Min	Art Unit:	1614
Application No.:	09/895,141	Examiner	P. G. Spivack
Filed:	June 29, 2001	Confirmation No.:	8276
Title:	LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT		

Mail Stop Petitions
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. § 1.181(a) FOR WITHDRAWAL OF HOLDING OF ABANDONMENT

Sir:

Applicants submit this Petition to the Commissioner under 37 C.F.R. § 1.181(a) for withdrawal of the holding of abandonment as set forth in the Notice of Abandonment mailed November 26, 2004, a copy of which accompanies the present petition.

CERTIFICATION UNDER 37 CFR §1.8
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service with sufficient postage as first class mail on this date, February 4, 2005, in an envelope addressed to: MAIL STOP Petitions, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Stephanie Sharrett *(Name of Person Mailing Paper)*
Stephanie Sharrett Feb. 4, 2005 *(Signature)* *(Date)*

GT\6427314.1
104662-101

REMARKS

The Notice of Abandonment mailed November 26, 2004 alleges that the above identified application was abandoned for failure to respond to the Office communication dated 10/7/2004 within the initial one month period. Applicants submit, however, that the Notice of Abandonment was premature and improper because extensions of time were available and, therefore, the period for reply had not yet ended.

The history of the present file includes the following communications: A non-final Office action was mailed on 8/7/2003 (Exhibit A). In Applicants' response to the Office action, mailed 12/5/2003 (Exhibit B), the pending claims were cancelled and new claims 23-32 were added. The Examiner mailed an Office communication on 3/15/2004 (Exhibit C) stating that Applicants' amendment was non-responsive with respect to the rejections set forth in the Office action because the new claims were directed to non-elected subject matter. In Applicants response mailed 4/15/2004 (Exhibit D), previously added claims 23-32 were canceled and the originally filed claims, revised to include additional limitations, where reinstated as new claims 33-43. In the Office communication mailed 10/7/2004 (Exhibit E), the Examiner alleged that Applicants' amendments were non-responsive, stating that the reinstated claims were directed to non-elected subject matter. A Notice of Abandonment was mailed on 11/26/2004 (Exhibit F) for failure to reply to the 10/7/2004 Office communication within the initial one month period.

Applicants respectfully submit that the time period for reply to the 10/07/04 Office communication included the initial one month period plus extensions of time under 37 CFR 1.136(a). In this regard, Applicants respectfully drawn attention to MPEP § 714.30, which states the following:

> Where the amendment is [a] bona fide [attempt to reply] but contains a serious omission, the examiner should: A) if there is sufficient time remaining for applicant's reply to be filed within the time period for reply to the non-final Office action (or within any extension pursuant to 37 CFR 1.136(a)), notify applicant that the omission must be supplied within the time period for reply; or B) if there is insufficient time remaining, issue an Office action setting a 1-month time period to complete the reply pursuant to 37 CFR 1.135(c).... If a new time period for reply is set pursuant to 37 CFR 1.135(c), applicant must supply the omission within this new time period for reply (*or any extensions under 37 CFR 1.136(a) thereof*) in order to avoid abandonment of the application. (emphasis added).

As such, the MPEP and the patent rules acknowledge that extensions of time, in addition to a one month period set for reply to a notice of a non-responsive amendment, are permitted where the Applicants' amendment is a bona fide attempt to reply and the time period for reply to the original Office action has expired.

Applicants further point out that extensions of time in this instance were expressly permitted by the Examiner in the Office communication dated 10/7/2004. It is stated in the Office communication, for example, that the amendment in Applicants' response mailed 4/15/2004 was a bona fide attempt to reply and Applicants were given a time period of one month or thirty days from the mailing date of the notice to reply. It is additionally stated in the Office communication that "EXTENSIONS OF THIS TIME PERIOD UNDER 37 CFR 1.136(a) ARE AVAILABLE." Furthermore, the time period for reply to the original Office action (mailed 8/7/2003) had expired. As such, it is submitted that the holding of abandonment was improper because extensions of time under 37 CFR 1.136(a) in the present instance are permitted by statute (see above) and Applicants were justified in relying on the Examiner's express grant of such extensions.

In sum, because extensions of time were permitted by statute and expressly granted by the Examiner in the Office communication mailed 10/7/2004, extensions of time were available as of 11/26/2004 and abandonment of the present application by the Examiner was improper. Accordingly, Applicants respectfully request that the holding of abandonment be withdrawn.

No fees are believed due for the submission of this petition. However, the Commissioner is hereby authorized to charge any fees associated with the filing submitted herewith, or credit any overpayment, to Deposit Account No. 07-1896.

Respectfully submitted,

Date: February 4, 2005

Reg. No. 52,182

0660

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 667-1456
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO CUSTOMER NO. 28213

Enclosure: Exhibits A, B, C, D, E

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,141	06/29/2001	Seymour Benzer	30431.3US01 CIT1560-1	8276

26941 7590 08/07/2003

MANDEL & ADRIANO
55 SOUTH LAKE AVENUE
SUITE 710
PASADENA, CA 91101

EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 08/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/895,141	Benzer et al.
Examiner	**Art Unit**
Phyllis G. Spivack	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 22, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above, claim(s) *12-22* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-11* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3, 10*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicants' Response to the Restriction Requirement filed May 22, 2003, Paper No. 9, is acknowledged. Applicants elected with traverse Group I, claims 1-11, which represent all of the claims presently under consideration.

No reasons for the traversal are advanced.

Claims 12-22 are withdrawn from consideration by the Examiner as being drawn to non-elected inventions, 37 C FR 1.142(b). Re-confirmation is requested when Applicants respond to this Office Action.

Two Information Disclosure Statements filed October 15, 2001 and February 12, 2002, respectively, Paper Nos. 3 and 10, are further acknowledged and have been reviewed.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the administration of 4-phenylbutyric acid to Drosophila, does not reasonably provide enablement for any subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims are directed to extending the life span of any subject. The specification provides support for extending the life span of Drosophila comprising administering one particular inhibitor of histone deacetylase.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to life span extension of any subject.

The relative skill of those in the art is generally that of a Ph.D or M.D.

Each particular "subject" has its own specific genetic characteristics. The broad recitation "extending the life span of a subject" is inclusive of many organisms that presently have no established successful therapies. In view of the specificity of the enzyme receptor for each particular inhibitor of histone deacetylase, a high degree of unpredictability would reasonably be expected.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any subject.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to Drosophila.

The quantity of experimentation necessary

Applicants have failed to provide guidance for subjects other than Drosophila and histone deacetylases other than 4-phenylbutyric acid. The skilled artisan would expect the interaction of a particular inhibitor of histone deacetylase to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding nor any criteria for extrapolating beyond the administration of 4-phenylbutyric acid to Drosophila. Absent reasonable *a priori* expectation of success for using a particular histone deacetylase inhibitor to extend the life span of subjects other than Drosophila, one skilled in the would have to test extensively many compounds to discover which particular histone deacetylase inhibitors exhibit efficacy in a particular subject. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Imai et al., Nature.

Imai teaches the administration of the potent inhibitor of histone deacetylase, trichostatin A, to extend the life span of yeast. See column 1 on page 797.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Nudelman et al., Journal of Medicinal Chemistry (abstract).

Nudelman teaches the administration of the histone deacetylase inhibitor glycerol tributyrate, a butyric acid derivative recited in claim 3, as an antitumor agent to extend the life span of the treated animal with a B16F0 melanoma primary cancer.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

Phyllis Spivack

August 6, 2003

PHYLLIS SPIVACK
PRIMARY EXAMINER

Notice of References Cited

Application/Control No.	Applicant(s)/Patent Under Reexam		
09/895,141	Benzer et al.		
Examiner	Art Unit	Page 1 of 1	
Phyllis G. Spivack	1614		

U.S. PATENT DOCUMENTS

		Document Number Country Code-Number-Kind Code	Date MM-YYYY[1]	Name	Classification[2]	
	A					
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

		Document Number Country Code-Number-Kind Code	Date MM-YYYY[1]	Country	Name	Classification[2]	
	N						
	O						
	P						
	Q						
	R						
	S						
	T						

NON-PATENT DOCUMENTS

		Include, as applicable: Author, Title, Date, Publisher, Edition or Volume, Pertinent Pages
	U	Nudelman et al., Journal of Medicinal Chemistry, 35(4), 687-94 (1992) (abstract).
	V	
	W	
	X	

* A copy of this reference is not being furnished with this Office action. See MPEP § 707.05(a). [1] Dates in MM-YYYY format are publication dates. [2] Classifications may be U.S. or foreign.

FORM 1449*	Docket Number	Application Number
INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION #3	30431.3US01	09/895,141
	Applicant: Seymour Benzer and Kyung-Tai Min	
(Use several sheets if necessary)	Filing Date: June 29, 2001	Group Art Unit: 1614

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

PS		Alfageme, C. R., Zweidler, A., Mahowald, A. & Cohen, L. H. Histones of *Drosophila* embryos *J. Biol. Chem.* 12, 3729-3736 (1974).
PS		Benzer, S. *Proc. Natl. Acad. Sci. U.S.A.* 58, 1112-1119 (1967).
DS		Guarente, L & Kenyon, C. *Nature* 408, 255-262 (2000).
PS		Imai, S., Amstrong, C. M., Kaeberlein, M. & Guarente, L. The transcriptional silencing and longevity protein Sir2 is an NAD-dependent histone deacetylase. *Nature* 403, 795-800 (2000).
PS		Kim, S., Benguria, A., Lai, C. & Jazwinski, S. M. Modulation of life-span by histone deacetylase genes in *Saccharomyces cerrevisiae Mol. Biol. Cell* 10, 3125-3136 (1999).
PS		Lea et al. Induction of Histone Acetylation and Growth Regulation in Erythroleukemia Cells by 4-phenylbutyrate and Structural Analogs *Anticancer Research* 19:1971-1976 (1999).
PS		Lea, M. A. & Randolph, V.M. Induction of reporter gene expression by inhibitors of histone deacetylase *Anticancer Res.* 18, 2717-2721 (1998).
PS		Lee, C. *et al.* Gene expression profile of aging and its retardation by caloric restriction *Science* 285, 1390-1393 (1999).
DS		Lin, Y. J., Seroude, L. & Benzer, S. Extended life-span and stress resistance in the *Drosophila* mutant *methuselah Science* 282, 943-946 (1998).
PS		Mannervik, B. The isoenzymes of glutathione transferase. *Adv. Enzymol. Relat. Areas Mol. Biol.* 57, 357-417 (1985).
PS		Orr, W. C. & Sohal, R. S. Extension of life-span by overexpression of superoxide dismutase and catalase in *Drosophila melanogaster. Science* 263, 1128-1130 (1994).
PS		Orr, W. C. & Sohal, R.S. Effects of Cu/Zn superoxide dismutase overexpresion on life span and resistance to oxidative stress in transgenic *Drosophila melanogaster. Arch. Biochem. Biophys.* 301, 34-40 (1993).
PS		Parkes, T. L. *et al.* Extension of *Drosophila* lifespan by overexpression of human SOD1 in motoneurons. *Nat. Genet.* 19, 171-174 (1998).
PS		Rogina, B., Reenan, R. A., Nilsen, S. P. & Helfand, S. L. Extended life-span conferred by cotransporter gene mutations in *Drosophila Science* 290, 2137-2140 (2000).
PS		Shelton, D. N. *et al.*, Microarray analysis of replicative senescence *Current Biology* 9, 939-945 (1999).
PS		Tatar, M., Khazaeli, A. A. & Curtsinger, J. W. Chaperoning extended life. *Nature* 390, 30 (1997).
PS		Webster, G. C. & Webster, S. L. Specific disappearance of translatable messenger RNA for elongation factor one in aging *Drosophila melanogaster. Mech. Ageing Devel.* 24, 335-342.
DS		Zou, S., Meadows, S., Sharp, L., Jan, L.Y. & Jan, Y. N. Genome-wide study of aging and oxidative stress response in *Drosophila melanogaster Proc. Natl. Acad. Sci. U.S.A.* 97. 13726-13731 (2000).

EXAMINER Phyllis Spivack DATE CONSIDERED 8/5/03

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

FORM 1449*

INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION

(Use several sheets if necessary)

Docket Number	Application Number
30431.3US01	09/895,141
Applicant	
Seymour Benzer and Kyung-Tai Min	
Filing Date	**Group Art Unit**
June 29, 2001	1614

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

PS		Lithgow, G. J. Temperature, stress response and aging. *Rev. Clin. Gerontol.* 6, 119-127 (1996) **(Exhibit 19)**
PS		Reiter et al. 2001, A Systematic Analysis of Human Disease-Associated Gene Sequences In *Drosophila melanogaster*. *Genome Research*, 11:1114-1125. **(Exhibit 20)**

EXAMINER	Phyllis Spivack	DATE CONSIDERED	8/5/03

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

ACCESSION NUMBER: 1992:98964 CAPLUS
DOCUMENT NUMBER: 116:98964
TITLE: Novel anticancer prodrugs of butyric acid. 2
AUTHOR(S): Nudelman, Abraham; Ruse, Margaretta; Aviram, Adina; Rabizadeh, Ester; Shaklai, Matityahu; Zimrah, Yael; Rephaeli, Ada
CORPORATE SOURCE: Chem. Dep., Bar-Ilan Univ., Ramat Gan, 52910, Israel
SOURCE: Journal of Medicinal Chemistry (1992), 35(4), 687-94
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antitumor activity of novel prodrugs of butyric acid was examd. The in vitro effect of the compds. on induction of cytodifferentiation and on inhibition of proliferation and clonogenicity showed that (pivaloyloxy)methyl butyrate (I) was the most active drug. Structure-activity relation study suggested that its activity stemmed from hydrolytically released butyric acid. In vivo, I displayed antitumor activity in B16F0 melanoma primary cancer model, manifested by a significant increase in the **life span** of the treated animals. Murine lung tumor burden, induced by injection of the highly metastatic melanoma cells (B16F10.9), was decrease byd I. It also displayed a significant therapeutic activity against spontaneous metastases which were induced by 3LL Lewis lung carcinoma cells. Moreover, I has the advantage of low toxicity, with an acute LD50 = 1.36 g/kg). I is a potential antineoplastic agent.

IT **60-01-5**, Glycerol tributyrate
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neoplasm inhibiting activity of, butyric acid prodrugs in relation to)

REVISED AMENDMENT PRACTICE: 37 CFR 1.121 CHANGED COMPLIANCE IS MANDATORY - Effective Date: July 30, 2003

All amendments filed on or after the effective date noted above must comply with revised 37 CFR 1.121. See Final Rule: **Changes To Implement Electronic Maintenance of Official Patent Application Records** (68 *Fed. Reg.* 38611 (June 30, 2003), posted on the Office's website at: http://www.uspto.gov/web/patents/ifw/ with related information. The amendment practice set forth in revised 37 CFR 1.121, and described below, replaces the voluntary revised amendment format available to applicants since February 2003. **NOTE: STRICT COMPLIANCE WITH THE REVISED 37 CFR 1.121 IS REQUIRED AS OF THE EFFECTIVE DATE (July 30, 2003).** The Office will notify applicants of amendments that are not accepted because they do not comply with revised 37 CFR 1.121 via a Notice of Non-Compliant Amendment. See MPEP 714.03 (Rev. 1, Feb. 2003). The non-compliant section(s) will have to be corrected and the entire corrected section(s) resubmitted within a set period.

Bold underlined italic font has been used below to highlight the major differences between the revised 37 CFR 1.121 and the voluntary revised amendment format that applicants could use since February, 2003.
Note: The amendment practice for **reissues** and **reexamination proceedings**, except for drawings, has not changed.

REVISED AMENDMENT PRACTICE

I. Begin each section of an amendment document on a separate sheet:
Each section of an amendment document (*e.g.*, Specification Amendments, Claim Amendments, Drawing Amendments, and Remarks) must begin on a separate sheet. Starting each separate section on a new page will facilitate the process of separately indexing and scanning each section of an amendment document for placement in an image file wrapper.

II. Two versions of amended part(s) no longer required:
37 CFR 1.121 has been revised to no longer require two versions (a clean version and a marked up version) of each replacement paragraph or section, or amended claim. Note, however, the requirements for a clean version and a marked up version for substitute specifications under 37 CFR 1.125 have been retained.

A) Amendments to the claims:
Each amendment document that includes a change to an existing claim, cancellation of a claim or submission of a new claim, **must include a complete listing** of all claims in the application. After each claim number in the listing, the status must be indicated in a parenthetical expression, and **the text of each pending claim** (with markings to show current changes) must be presented. The claims in the listing will replace all prior claims in the application.

(1) The current status of all of the claims in the application, including any previously canceled, not entered or withdrawn claims, must be given in a parenthetical expression following the claim number using only one of the following seven status identifiers: (original), (currently amended), (canceled), (withdrawn), (new), *(previously presented) and (not entered).* The text of all pending claims, *including withdrawn claims,* must be submitted each time any claim is amended. Canceled *and not entered* claims must be indicated by only the claim number and status, without presenting the text of the claims.

(2) The text of all claims being currently amended must be presented in the claim listing with markings to indicate the changes that have been made relative to the immediate prior version. The changes in any amended claim must be shown by underlining (for added matter) or strikethrough (for deleted matter) with 2 exceptions: (1) for *deletion of five characters or fewer, double brackets may be used (e.g., [[eroor]]); and (2) if strikethrough cannot be easily perceived (e.g., deletion of the number "4" or certain punctuation marks), double brackets must be used (e.g., [[4]]). As an alternative to using double brackets, however, extra portions of text may be included before and after text being deleted, all in strikethrough, followed by including and underlining the extra text with the desired change* (e.g., ~~*number 4 as*~~ *number 14 as)*. An accompanying clean version is not required and should not be presented. Only claims of the status "currently amended," and "withdrawn" that are being amended, may include markings.

(3) The text of pending claims not being currently amended, *including withdrawn claims,* must be presented in the claim listing in clean version, *i.e.*, without any markings. Any claim text presented in clean version will constitute an assertion that it has not been changed relative to the immediate prior version except to omit markings that may have been present in the immediate prior version of the claims.

GRAY CARY WARE & FREIDENRICH 401 B STREET, SUITE 2000 SAN DIEGO, CA 92101 **CHECK NO.:** **549587**

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PATENT ATTORNEY DOCKET NO.: CIT1560-1
The Patent and Trademark Office date stamp sets forth the receipt date of:
Applicant or Patentee: Benzer et al. **Filing or Issue Date**: June 29, 2001
Serial No.: 09/895,141
Title: LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT

[X] Transmittal Letter (2 pgs)
[ ] Preliminary Amendment (pages)
[X] Response to Office Action (9 pages w/Ex. A)
[ ] Issue Fee [ ] Request Patent Copies
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[] Drawings: Sheets (informal)
[] Declaration (pg.)
[] Small Entity Statement
[] Power of Attorney (pg.)
[] Assignment/Recordal Cover Sheet (pg.)
[] Copy of Notice to File Missing Parts
[ ] Information Statement (pgs.)
[ ] Form PTO-1449 (pg.)
[ ] Number of References ( )
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[X] Petition for 1 Month Extension of Time (2 pgs)
[] Status Inquiry (pg.)
[] Certificate of Correction (pg.)
[] Notice of Appeal (pg.)
[] ~~Appeal~~ Brief ( )

Date Mailed: 12/08/03
Date Due: 12/08/03

PATENT
Attorney Docket No.: CIT1560-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Benzer et al.	Art Unit:	1614
Serial No.:	09/895,141	Examiner	Phyllis G. Spivack
Filed:	June 29, 2001		
Title:	LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT		

Mail Stop: Non-Fee Amendment
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL SHEET

Sir:

Transmitted herewith for the above-identified application, please find:

1. Response to the Office Action mailed August 7, 2003 (8 pages); including Exhibit A (1 page);

2. Petition for One Month Extension of Time (2 pages);

3. Check No.: 549587 in the amount of $55.00; and

4. Return Receipt Postcard.

CERTIFICATION UNDER 37 CFR §1.8

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, December 5, 2003, in an envelope addressed to: Mail Stop Non-Fee Amendment, Commissioner for Patents and Trademarks, P. O. Box 1450, Alexandria, VA 22313-1450.

Cara Grifone
Name of Person Mailing Paper

Cara Grifone
Signature

Gray Cary\GT\6373151.1
104662-101

A check in the amount of $55.00 is enclosed for the One Month Extension of Time fee. If any additional fee is required, the Commissioner is hereby authorized to charge, or credit any overpayments to Deposit Account No. 50 -1355. A duplicate copy of this sheet is attached.

Respectfully submitted,

Date: December 5, 2003

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 667-1456
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213

PATENT
Attorney Docket No.: CIT1560-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Benzer et al.	Art Unit:	1614
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Mail Stop: Non-Fee Amendment
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

PETITION FOR EXTENSION OF TIME

Sir:

This is a request under the provisions of 37 C.F.R. § 1.136(a) to extend the period for responding to the Office Action mailed August 7, 2003.

The requested extension is for one (1) month, extending the period for response to December 7, 2003.

CERTIFICATION UNDER 37 CFR §1.8

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, December 5, 2003, in an envelope addressed to: Mail Stop Non-Fee Amendment, Commissioner for Patents and Trademarks, P. O. Box 1450, Alexandria, VA 22313-1450.

Cara Grifone
Name of Person Mailing Paper

Signature

Gray Cary\GT\6377307.1
104662-101

A check in the amount of $55.00 is enclosed for the Petition for One Month Extension of Time fee. The Commissioner is hereby authorized to charge any additional fees associated with the filing submitted herewith, or credit any overpayment, to Deposit Account No. 50-1355. A copy of the Transmittal is enclosed.

Respectfully submitted,

Date: December 5, 2003

Lisa Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
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PATENT
Attorney Docket No.: CIT1560-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Benzer et al.	Art Unit:	1614
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Mail Stop: Non-Fee Amendment
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT IN RESPONSE TO THE OFFICE ACTION

Sir:

Responsive to the Office Action mailed August 7, 2003, reconsideration of the application in view of the new claims and following remarks is respectfully requested.

CERTIFICATION UNDER 37 CFR §1.8

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, December 5, 2003, in an envelope addressed to: Mail Stop Non-Fee Amendment, Commissioner for Patents and Trademarks, P. O. Box 1450, Alexandria, VA 22313-1450.

Cara Grifone
Name of Person Mailing Paper

Cara Grifone
Signature

Gray Cary\GT\6368604.2
104662-101

I. AMENDMENTS

Please cancel claims 1-22 and add new claims 23-32, as indicated below. Upon entry of the present amendment, the claims will stand as follows. The following listing of claims will replace all prior versions and listings of the claims in the present application:

1 to 22. (Canceled)

23. (New) A method for promoting free radical resistance of a cell comprising, contacting an inhibitor of histone deacetylase with the cell in an amount effective to increase activity of genes associated with free radical resistance selected from the group consisting of superoxide dismutase, cytochrome P450, and glutathione S transferase, thereby promoting free radical resistance of the cell.

24. (New) The method of claim 23, wherein the inhibitor of histone deacetylase is a butyric acid derivative.

25. (New) The method of claim 24, wherein the butyric acid derivative is selected from the group consisting of isobutyramide, monobutyrin, tributyrin, 2-phenylbutyric acid, 3-phenylbutyric acid, 4-phenylbutyric acid (PBA), phenylacetic acid, cinnamic acid, alpha-methyldihydrocinnamic acid, 3-chloropropionic acid and vinyl acetic acid.

26. (New) The method of claim 25, wherein the butyric acid derivative is soluble in an aqueous solution.

27. (New) The method of claim 25, wherein the butyric acid derivative is a salt.

28. (New) The method of claim 23, wherein the cell is a cell of an invertebrate organism.

29. (New) The method of claim 28, wherein the invertebrate organism is an insect or a nematode.

30. (New) The method of claim 29, wherein the insect is a Drosophila.

31. (New) The method of claim 23, wherein the cell is a cell of a vertebrate organism.

32. (New) The method of claim 31, wherein the vertebrate organism is selected from the group consisting of an amphibian, human, equine, porcine, bovine, murine, canine, feline, and avian organism.

II. REMARKS

Upon entry of the new claims, claims 23-32 will be pending. Claims 1-22 have been cancelled herein.

A. Regarding the Amendments

Claims 1-22 are cancelled herein without disclaimer and without prejudice.

New claims 23-33 have been added. The new claims are supported, for example, by Example 1(F) at page 20, lines 1-15, and Example 2, pages 20-28. Example 1(F) describes experiments involving induction of resistance to the free radical generator paraquat in Drosophila by treatment with an inhibitor of histone deacetylase. Example 2 illustrates induction of genes by treatment with a histone deacetylase inhibitor, including genes involved in free radical or oxidative stress. Table 2 at pages 22-25, and Table 3 at page 28, illustrate genes induced by treatment with 4-phenylbutyrate according to Example 2. Claims 24-27 are supported by original claims 2-5, respectively. Claims 29-33 are further supported, for example, at page 6, lines 27-31. As such, new claims 23-33 do not add new matter.

B. Regarding the Restriction Requirement

Applicants acknowledge the election of Group I, consisting of claims 1-11, and withdrawal of claims 12-22 from consideration by the Examiner as being drawn to non-elected inventions. However, in order to focus the claims on the elected group, claims 12-22 have been cancelled herein.

C. **Rejection Under 35 U.S.C. § 112**

The objection to the specification and corresponding rejection of claims 1-7 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement are respectfully traversed. Claims 1-7 have been cancelled, thereby rendering the rejection moot. However, in order to be fully responsive to the Office Action, Applicants will address the rejection as to new claims 23-33.

It is acknowledged in the Office Action that the specification is enabling for extending the life span of a Drosophila by administering the histone deacetylase inhibitor 4-phenylbutyric acid. It is alleged, however, that the specification provides no guidance for subjects other than Drosophila or histone deacetylase inhibitors other than 4-phenylbutyric acid. As such, it is alleged that undue experimentation would have been required for one skilled in the art to practice the claimed methods.

However, Applicants submit, with respect to the currently claimed methods, that Drosophila is currently accepted by the scientific community as a model system that is predictive of outcomes in other organisms. For example, the specification discloses that the Drosophila is an accepted model organism for the study of disease in other organisms (see, for example, page 13, line 26, to page 14, line 16). The specification further discloses that the effects of the histone deacetylase inhibitor 4-phenylbutyric acid in Drosophila, as described in the current specification, are consistent with molecular effects of histone deacetylase inhibition in other organisms, such as yeast (see, for example, paragraph bridging pages 13 and 14). As such, Applicants assert that one skilled in the art, viewing the specification, would have recognized that the currently claimed methods, as exemplified in Drosophila, would reasonably be effective in promoting free radical resistance in cells of other organisms.

In further support of this position, Applicants point out that there is no reason to believe that the exemplified method of promoting free radical resistance of an insect cell by contacting the cell with an inhibitor of histone deacetylase would not similarly be effective with respect to other types of cells. For example, Lea et. al. (Anticancer Res. 1999 May-Jun. 19(3A): 1971-6, a copy of which is attached as Exhibit A), describe use of 4-phenylbutyrate, the same compound exemplified in the current specification, and structural analogs, to effectively inhibit histone deacetylase in several

different cell types, as well as produce the similar downstream effect of inhibiting cell growth. For example, Lea et. al. reported that 4-phenylbutyrate inhibited histone deacetylase in both mouse erythroleukemia cells and human leukemic cells inhibited growth of these cells. Lea et al. further reported that other compounds, including structural analogs of 4-phenylbutyrate, similarly inhibited histone deacetylase in such cells. Applicants point out that Lea et. al. is cited in the current specification at page 20, lines 20-23. Thus, the results reported by Lea et al. confirm that, as disclosed in the subject application, agents that inhibit histone deacetylase effectively decrease histone acetylation in multiple cell types and produce similar downstream effects. As such, it is submitted that undue experimentation would not have been required for one skilled in the art to promote free radical resistance of various types of cells and organisms containing such cells by contacting such cells with an inhibitor of histone deacetylase to increase activity of genes associated with free radical resistance selected from superoxide dismutase, cytochrome P450, and glutathione S transferase, thereby promoting free radical resistance of the cell.

In summary, the specification discloses that an inhibitor of histone deacetylase can promote free radical resistance of a cell, and exemplifies the claimed methods using the compound 4-phenylbutyrate in Drosophila cells. The Specification also teaches that Drosophila cells are a model system predictive of outcomes in other organisms. As such, it is submitted that one skilled in the art, viewing the subject application, would have known how to practice the claimed methods without undue experimentation, and further that other histone deacetylate inhibiting compounds would be effective for increasing activity of genes associated with free radical resistance in a method of the invention when used in various types of cells and organisms containing such cells. Accordingly, it is respectfully requested that the Examiner reconsider and remove the rejection of the claims under 35 U.S.C. § 112, first paragraph.

D. Prior Art Rejections

The Examiner has rejected claim 1 under 35 U.S.C. § 102(a) as being anticipated by Imai et al., Nature 403, 795-800 (2000). Applicants have cancelled Claim 1 rendering the rejection moot. However, in order to be fully responsive to the rejection, Applicants traverse and address the rejection with respect to new claims 23-32.

Rejection of a claim under 35 U.S.C. § 102(a) requires that the reference describe all of the elements and all of the limitations of the rejected claim. The current claims are directed to a method of promoting free radical resistance of a cell by contacting an inhibitor of histone deacetylase with the cell in an amount effective to increase activity of genes associated with free radical resistance selected from the group consisting of superoxide dismutase, cytochrome P450, and glutathione S transferase, thereby promoting free radical resistance of the cell. Imai et al. describe the administration of trichostatin to extend the life span of yeast. As such, the teachings of Imai et al. do not include promoting free radical resistance of a cell by the administration of a histone deacetylase in an amount effective to increase activity of genes encoding superoxide dismutase, cytochrome P450, or glutathione S transferase.

Therefore, Imai et al. fail to disclose each and every element of the claims as now presented. As such, Applicants respectfully request that the rejection be withdrawn.

The Examiner has rejected claims 1-5 under 35 U.S.C. § 102(b) as being anticipated by Nudelman et al., Journal of Medicinal Chemistry (abstract). Claims 1-5 have been cancelled, thereby rendering the rejection moot. In order to be fully responsive to the rejection, however, Applicants traverse and address the rejection with respect to new claims 23-32.

The rejection of a claim under 35 U.S.C. § 102(b) requires that the reference describe all of the elements and limitations of the rejected claim. Nudelman et al. describe the administration of the histone deacetylase inhibitor glycerol tributyrate as an antitumor agent, thereby extending the life span of a treated animal having a B16F0 melanoma primary cancer. However, Nudelman et al. do not teach a method of promoting free radical resistance of a cell by contacting the cell with an

inhibitor of histone deacetylase to increase activity of genes encoding superoxide dismutase, cytochrome P450, or glutathione S transferase, as currently claimed in the present invention.

Therefore, because Nudelman et al. fail to disclose all the elements of the currently claimed methods, withdrawal of the rejection is respectfully requested.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Acct. No. 50-1355.

Respectfully submitted,

Date: December 5, 2003

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 667-1456
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
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Enclosure: Exhibit A

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1: Anticancer Res. 1999 May-Jun;19(3A):1971-6. Related Articles, Link

Induction of histone acetylation and growth regulation in eryrthroleukemia cells by 4-phenylbutyrate and structural analogs.

Lea MA, Randolph VM, Hodge SK.

Department of Biochemistry and Molecular Biology, UMDNJ-New Jersey Medical School, Newark 07103, USA. lea@umdnj.edu

The objective of this investigation was to study the relationship between histone acetylation and growth inhibition by 4-phenylbutyrate and structural analogs. Inhibition of growth of DS19 mouse erythroleukemia cells and K56 human leukemic cells by 4-phenylbutyrate did not appear to be mediated by glutamine depletion. Vanadate blocked differentiation of DS19 cells but did not affect the hyperacetylation of histones. 2-phenylbutyrate was a more effective inhibitor of cell proliferation than 3-phenylbutyrate but was less effective as an inducer of histone acetylation. 4-Phenylbutyrate was a more effective inhibitor of histone deacetylase and inducer of histone acetylation than the structural analogs examined including 2- and 3-phenylbutyrate, cinnamate, methoxycinnamate, 2-phenoxybutyrate and phenoxyacetate.

PMID: 10470142 [PubMed - indexed for MEDLINE]

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THE FACE OF THIS DOCUMENT HAS A COLORED BACKGROUND ON WHITE PAPER

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PATENT ATTORNEY DOCKET NO.: CIT1560-1
The Patent and Trademark Office date stamp sets forth the receipt date of:
Applicant or Patentee: Benzer et al. **Filing or Issue Date**: June 29, 2001
Serial No.: 09/895,141
Title: LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,141	06/29/2001	Seymour Benzer	30431.3US01	8276

26941 7590 03/15/2004

MANDEL & ADRIANO
55 SOUTH LAKE AVENUE
SUITE 710
PASADENA, CA 91101

EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

The reply filed on December 12, 2003 is not responsive to the prior Office Action because of the following matter. Newly submitted claims 23-32 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Methods for promoting free radical resistance of a cell comprising contacting an inhibitor of histone deacetylase to increase activity of genes associated with free radical resistance selected from the group consisting of superoxide dismutase, cytochrome P450 and glutathione S tranferase require futher search and different considerations.

Since Applicants have received an Action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicants are given **ONE (1) MONTH or THIRTY (30) DAYS** from the mailing date of this notice, whichever is longer, within which to supply the correction in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136(a).

Any inquiry concerning this communication should be directed to Phyllis G. Spivack at telephone number 571-272-0585.

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

March 11, 2004

PHYLLIS SPIVACK
PRIMARY EXAMINER

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,141	06/29/2001	Seymour Benzer	30431.3US01	8276

CIT1560-1

EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

26941 7590 03/15/2004

MANDEL & ADRIANO
55 SOUTH LAKE AVENUE
SUITE 710
PASADENA, CA 91101

MAR 29 2004

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

The reply filed on December 12, 2003 is not responsive to the prior Office Action because of the following matter. Newly submitted claims 23-32 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Methods for promoting free radical resistance of a cell comprising contacting an inhibitor of histone deacetylase to increase activity of genes associated with free radical resistance selected from the group consisting of superoxide dismutase, cytochrome P450 and glutathione S tranferase require futher search and different considerations.

Since Applicants have received an Action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. See 37 CFR 1.142(b) and MPEP § 821.03.

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Any inquiry concerning this communication should be directed to Phyllis G. Spivack at telephone number 571-272-0585.

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

March 11, 2004

PHYLLIS SPIVACK
PRIMARY EXAMINER

MANDEL & ADRIANO

INTELLECTUAL PROPERTY ATTORNEYS

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PASADENA, CALIFORNIA 9110 1
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To: Dr. Scott Carter
Company, Firm, or Institution: CIT
Facsimile No.: 626-356-2486
Your Ref: CIT 3155

CIT1560-1

cc: Lisa Haile, Esq.
Company, Firm, or Institution: Gray Cary
Facsimile No.: 858-677-1465
Your Ref: Unknown

From: Richelle Domingo
Date: March 26, 2004
Total No. of pages (including this page): 4
M&A Ref: 30431.3US01

COMMENTS:

MANDEL & ADRIANO

INTELLECTUAL PROPERTY ATTORNEYS

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*Admitted in New York Only

March 26, 2004

By Facsimile: 626/356 2486
Scott Carter, Ph.D.
Licensing Associate
California Institute of Technology
Mail Code: 201-85
1200 East California Blvd.
Pasadena, California 91125

Re: U.S. Serial No. 09/895,141 filed June 29, 2001
Entitled: "LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT"
Inventors: Seymour Benzer and Kyung-Tai Min
CIT Case No. CIT 3155
M&A Ref: 30431.3US01

Dear Dr. Carter:

I enclose a copy of the March 15, 2004, Communication from the US Patent and Trademark Office.

Today, we will forward the original document to Ms. Lisa Haile, of Gray Cary pursuant to your October 2, 2001 letter.

Other than forwarding all communications from the PTO to you, we will do nothing more in connection with this case.

Sincerely,

Richelle

Richelle Ann Domingo
Legal Assistant

/rapd
Enclosure
cc: Lisa Haile, Esq. (w/ encl, by facsimile: 858-677-1465, original by mail)
SaraLynn Mandel, Esq. (w/o encl.)
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The Patent and Trademark Office date stamp sets forth the date of receipt of:

Applicant(s): Benzer and Min
Application No.: 09/895,141
Filing Date: June 29, 2001
Confirmation No.: 8276
Title: LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT

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- ☒ Exhibit A (1 pg.)
- ☒ Return Receipt Postcard

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Date Mailed: 04/15/2004
Date Due: 04/15/2004

PATENT
Attorney Docket No.: CIT1560-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Benzer and Min	Art Unit:	1614
Application No.:	09/895,141	Examiner	P. G. Spivack
Filed:	June 29, 2001	Confirmation No.:	8276
Title:	LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT		

MAIL STOP NON-FEE AMENDMENT
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Sir:

Transmitted herewith for the above-identified application please find:

1. Amendment in Response to the Office Action mailed March 15, 2004 (8 pgs.);
2. Exhibit A (1 pg.); and
3. Return Receipt Postcard.

CERTIFICATION UNDER 37 CFR §1.8
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service with sufficient postage as first class mail on this date, **April 15, 2004**, in an envelope addressed to: MAIL STOP NON-FEE AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Gregory P. Austin *(Name of Person Mailing Paper)*
Gregory P. Austin *(Signature)* — April 15, 2004 *(Date)*

Gray Cary\GT\6395668.1
104662-101

Applicants claim **SMALL ENTITY status** in the above-identified application. Pursuant to 37 C.F.R. § 1.27, a verified statement claiming small entity status in not required.

The Fee for this Response is calculated as follows:

For	Claims Remaining After Amendment	Highest Number Previously Paid For	Extra Claims	Small Entity Rate	Large Entity Rate	Calculations
Total Claims	11	22	0	x $09	x $18	$0
Independent Claims	1	4	0	x $43	x $86	$0
					TOTAL FEE	$0

No fee is deemed necessary in connection with the filing of this communication. However, if a fee is required, the Commissioner is hereby authorized to charge any required fee associated with this communication, or credit any overpayments, to Deposit Account No. 50-1355. A duplicate copy of this letter is enclosed.

Respectfully submitted,

Date: April 15, 2004

June M. Learn

June M. Learn, J.D., Ph.D.
Registration No. 31,238
Telephone: (858) 677-1416
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
USPTO CUSTOMER NO. 28213

PATENT
Attorney Docket No.: CIT1560-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Benzer and Min	Art Unit:	1614
Application No.:	09/895,141	Examiner	P. G. Spivack
Filed:	June 29, 2001	Confirmation No.:	8276
Title:	LIFE EXTENSION OF DROSOPHILA BY A DRUG TREATMENT		

MAIL STOP NON-FEE AMENDMENT
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT IN RESPONSE TO THE OFFICE ACTION

Sir:

Responsive to the Office Action mailed August 7, 2003, and further responsive to the Office Action mailed March 15, 2004, reconsideration of the application in view of the following amendments and remarks is respectfully requested.

Amendments to the Claims are reflected in the listing of claims which begins on page two of this paper.

Remarks/Arguments begin on page four of this paper.

CERTIFICATION UNDER 37 CFR §1.8
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service with sufficient postage as first class mail on this date, **April 15, 2004**, in an envelope addressed to: MAIL STOP NON-FEE AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Gregory P. Austin *(Name of Person Mailing Paper)*
Gregory P. Austin *(Signature)* **April 15, 2004** *(Date)*

Gray Cary\GT\6395610.1
104662-101

I. AMENDMENTS

In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Upon entry of the present amendment, the claims will stand as follows:

Please cancel claims 23-32 without prejudice.

Claims 1 to 32. (Canceled)

33. (New) A method for extending the life span of an organism comprising administering an inhibitor of histone deacetylase to the subject in an amount effective to increase activity of at least one gene encoding a protein selected from superoxide dismutase, cytochrome P450, or glutathione S transferase to extend the life span of the organism.

34. (New) The method of claim 33, wherein the inhibitor of histone deacetylase is a butyric acid derivative.

35. (New) The method of claim 34, wherein the butyric acid derivative is selected from the group consisting of isobutyramide, monobutyrin, tributyrin, 2-phenylbutyric acid, 3-phenylbutyric acid, 4-phenylbutyric acid (PBA), phenylacetic acid, cinnamic acid, alpha-methyldihydrocinnamic acid, 3-chloropropionic acid and vinyl acetic acid.

36. (New) The method of claim 35, wherein the butyric acid derivative is soluble.

37. (New) The method of claim 35, wherein the butyric acid derivative is a salt.

38. (New) The method of claim 33, wherein the inhibitor of histone deacetylase is PBA and PBA is a salt.

39. (New) The method of claim 33, wherein the subject is a mutant organism.

40. (New) The method of claim 33, wherein the organism is a Drosophila.

41. (New) The method of claim 40, wherein the Drosophila is a Drosophila melanogaster.

42. (New) The method of claim 41, wherein the Drosophila melanogaster is w^{1118}.

43. (New) The method of claim 40, wherein the Drosophila is a mutant Drosophila.

II. REMARKS

Claims 1-32 have been presented in this application. All subject matter, except that of original claims 1-11 has been determined by the Examiner to be drawn to non-elected subject matter. Applicants have previously cancelled claims 1-22. Claims 23-32, were not entered by the Examiner and are cancelled by the present communication without prejudice. To more particularly define the subject matter of the elected invention, Applicants have added new claims 33-43, which incorporate the subject matter of original claims 1-11. The new claims add no new matter, being fully supported by the Specification and original claims 1-11 of this application. Upon entry of the present amendment, claims 33-43 will be pending in this application.

C. The Rejection Under 35 U.S.C. § 112

The objection to the specification and corresponding rejection of claims 1-7 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement are respectfully traversed. Claims 1-7 have been cancelled, thereby rendering the rejection moot. However, in order to be fully responsive to the Office Action, Applicants will address the rejection as to new claims 33-43.

It is acknowledged in the Office Action that the specification is enabling for extending the life span of a Drosophila by administering the histone deacetylase inhibitor 4-phenylbutyric acid. It is alleged, however, that the specification provides no guidance for subjects other than Drosophila or histone deacetylase inhibitors other than 4-phenylbutyric acid. As such, it is alleged that undue experimentation would have been required for one skilled in the art to practice the claimed methods.

However, Applicants submit that Drosophila is currently accepted by the scientific community as a model system that is predictive of outcomes in other organisms. For example, the specification discloses that the Drosophila is an accepted model organism for the study of disease in other organisms (see, for example, page 13, line 26, to page 14, line 16). The specification further discloses that the effects of the histone deacetylase inhibitor 4-phenylbutyric acid in Drosophila, as described in the current specification, are consistent with molecular effects of histone deacetylase

inhibition in other organisms, such as yeast (see, for example, paragraph bridging pages 13 and 14). Therefore, Applicants submit that one skilled in the art, viewing the specification, would have recognized that the currently claimed methods, as exemplified in Drosophila, would reasonably be effective to increase activity of at least one gene encoding a protein selected from superoxide dismutase, cytochrome P450, or glutathione S transferase to extend the life span of other organisms.

In further support of this position, Applicants point out that there is no reason to believe that the exemplified method of extending the life span of an organism by contacting the cell with an inhibitor of histone deacetylase would not similarly be effective with respect to other types of organisms containing genes that encode a protein selected from superoxide dismutase, cytochrome P450 or glutathione S transferase. For example, Lea et. al. (Anticancer Res. 1999 May-Jun. 19(3A): 1971-6, a copy of which is attached as Exhibit A), describe use of 4-phenylbutyrate, the same compound exemplified in the current specification, and structural analogs, to effectively inhibit histone deacetylase in several different cell types, as well producing the similar downstream effect of inhibiting cell growth. For example, Lea et. al. reported that 4-phenylbutyrate inhibited histone deacetylase in both mouse erythroleukemia cells and human leukemic cells thereby inhibiting growth of these cells.

Lea et al. further reported that other compounds, including structural analogs of 4-phenylbutyrate, similarly inhibited histone deacetylase in such cells. Applicants point out that Lea et. al. is cited in the current specification at page 20, lines 20-23. The results reported by Lea et al. confirm that, as disclosed in the subject application, agents that inhibit histone deacetylase effectively decrease histone acetylation in multiple cell types and produce downstream effects similar to those reported for 4-phenylbutyrate in the cells of various organisms. Accordingly, Applicants submit that undue experimentation would not required for one skilled in the art to practice the invention, using the guidelines and procedures presented in the specification to extend the life span of various types of cells and other organisms. For example, those of skill in the art would know how to contact an organism with an inhibitor of histone deacetylase to increase activity of genes associated with free radical resistance selected from superoxide dismutase, cytochrome P450, and glutathione S transferase.

As is well known in the art, free radical activity in living organisms is a leading cause of aging, and disease. Hence, utilizing the invention methods that promote free radical resistance, those of skill in the art would readily succeed in extending the life span of the organism treated according to the invention methods.

In summary, the specification discloses that an inhibitor of histone deacetylase can promote free radical resistance of a cell so as to extend the life span of the organism, and exemplifies the claimed methods using the compound 4- phenylbutyrate in Drosophila cells. The Specification also teaches that Drosophila cells are a model system predictive of outcomes in other organisms.

Accordingly, it is submitted that one skilled in the art, viewing the subject application, would have known how to practice the claimed methods without undue experimentation, and further that histone deacetylate inhibiting compounds other than 4-phenylbutyric acid would be effective for increasing activity of genes associated with free radical resistance to extend the life of treated organisms. Accordingly, it is respectfully requested that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112, first paragraph.

D. Prior Art Rejections

Applicants respectfully traverse the rejection of claim 1 under 35 U.S.C. § 102(a) as being anticipated by Imai et al., Nature 403, 795-800 (2000). Claim 1 has been cancelled, thereby rendering the rejection moot. However, in order to be fully responsive to the Office Action, Applicants will address the rejection as to new claims 33-43.

Rejection of a claim under 35 U.S.C. § 102(a) requires that the reference describe all of the elements and all of the limitations of the rejected claim. The current claims are directed to a method of extending the life span of an organism by administration of an effective amount of an inhibitor of histone deacetylase. Applicants teach that an effective amount of a histone deacetylase inhibitor is an amount sufficient to increase activity of genes associated with free radical resistance. Such genes are disclosed as including genes that lead to expression of superoxide dismutase, cytochrome P450, and

glutathione S transferase. By contrast, Imai et al. describe the administration of trichostatin to extend the life span of yeast. The teachings of Imai et al. do not describe extending life span of an organism by administration of a histone deacetylase inhibitor in an amount effective to increase activity of genes encoding superoxide dismutase, cytochrome P450, or glutathione S transferase.

Therefore, as Imai et al. fail to disclose each and every element of claims 33-43 as now presented, Applicants submit that anticipation has not been established over Imai et al. As such, Applicants respectfully request reconsideration and withdrawal of the rejection.

Applicants further traverse the rejection of claims 1-5 under 35 U.S.C. § 102(b) as being anticipated by Nudelman et al., Journal of Medicinal Chemistry (abstract). Claims 1-5 have been cancelled, thereby rendering the rejection moot. However, in order to be fully responsive to the Office Action, Applicants will address the rejection as to new claims 33-43.

The rejection of a claim under 35 U.S.C. § 102(b) requires that the reference describe all of the elements and limitations of the rejected claim. Nudelman et al. describe the administration of the histone deacetylase inhibitor glycerol tributyrate as an antitumor agent, thereby extending the life span of a treated animal having a B16F0 melanoma primary cancer. However, Nudelman et al. do not teach a method of extending life span of an organism by administration of an inhibitor of histone deacetylase to increase activity of genes encoding superoxide dismutase, cytochrome P450, or glutathione S transferase, as currently claimed in the present invention.

Therefore, because Nudelman et al. fail to disclose all the elements of the currently claimed methods, Applicants respectfully submit that anticipation has not been shown over Nudelman et al. Reconsideration and withdrawal of the rejection, therefore, are respectfully requested.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Respectfully submitted,

Date: April 15, 2004

June M. Learn, J.D., Ph.D.
Registration No. 31,238
Telephone: (858) 667-1416
Facsimile: (858) 677-1465

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San Diego, California 92121-2133
USPTO CUSTOMER NO. 28213

Enclosure: Exhibit A

Text Version

Entrez PubMed Overview
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PubMed Services
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Cubby

Related Resources
Order Documents
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

Privacy Policy

1: Anticancer Res. 1999 May-Jun;19(3A):1971-6. Related Articles, Link

Induction of histone acetylation and growth regulation in eryrthroleukemia cells by 4-phenylbutyrate and structural analogs.

Lea MA, Randolph VM, Hodge SK.

Department of Biochemistry and Molecular Biology, UMDNJ-New Jersey Medical School, Newark 07103, USA. lea@umdnj.edu

The objective of this investigation was to study the relationship between histone acetylation and growth inhibition by 4-phenylbutyrate and structural analogs. Inhibition of growth of DS19 mouse erythroleukemia cells and K56 human leukemic cells by 4-phenylbutyrate did not appear to be mediated by glutamine depletion. Vanadate blocked differentiation of DS19 cells but did not affect the hyperacetylation of histones. 2-phenylbutyrate was a more effective inhibitor of cell proliferation than 3-phenylbutyrate but was less effective as an inducer of histone acetylation. 4-Phenylbutyrate was a more effective inhibitor of histone deacetylase and inducer of histone acetylation than the structural analogs examined including 2- and 3-phenylbutyrate, cinnamate, methoxycinnamate, 2-phenoxybutyrate and phenoxyacetate.

PMID: 10470142 [PubMed - indexed for MEDLINE]

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,141	06/29/2001	Seymour Benzer	30431.3US01	8276

26941 7590 10/07/2004

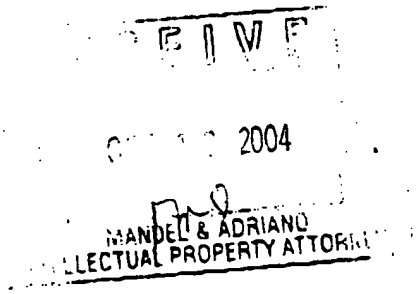
MANDEL & ADRIANO
55 SOUTH LAKE AVENUE
SUITE 710
PASADENA, CA 91101

EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 10/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.



PTO-90C (Rev. 10/03)

626 395 0694 U.S. Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT	PAPER
	100404

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

The Amendment filed on April 19, 2004 canceling all claims drawn to the elected invention and presenting only claims drawn to a non-elected invention is non-responsive (MPEP § 821.03). There are no remaining claims that are not readable on the elected invention. Newly submitted claims 33-43, drawn to methods for extending the life span of an organism comprising administering an inhibitor of histone deacetylase to increase activity of at least one gene encoding a protein selected from superoxide dismutase, cytochrome P450 or glutathione S transferase, are directed to an invention that is independent or distinct from the invention originally claimed. The new subject matter requires further search and consideration.
Since the above-mentioned Amendment appears to be a bona fide attempt to reply, Applicants are given a TIME PERIOD of ONE (1) MONTH or THIRTY (30) DAYS, whichever is longer, from the mailing date of this notice within which to supply the omission or correction in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD UNDER 37 CFR 1.136(a) ARE AVAILABLE.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 571-272-0585.

Phyllis Spivack

October 4, 2004

Phyllis Spivack
Primary Examiner
Art Unit 1614

PHYLLIS SPIVACK
PRIMARY EXAMINER

PTO-90C (Rev.04-03)

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,141	06/29/2001	Seymour Benzer	30431.3US01	8276

26941 7590 11/26/2004

MANDEL & ADRIANO
55 SOUTH LAKE AVENUE
SUITE 710
PASADENA, CA 91101

EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Notice of Abandonment	Application No.	Applicant(s)	
	09/895,141	BENZER ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

This application is abandoned in view of:

1. ☒ Applicant's failure to timely file a proper reply to the Office letter mailed on *07 October 2004*.
   (a) ☐ A reply was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply (including a total extension of time of _____ month(s)) which expired on _____.
   (b) ☐ A proposed reply was received on _____, but it does not constitute a proper reply under 37 CFR 1.113 (a) to the final rejection.
   (A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114).
   (c) ☐ A reply was received on _____ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
   (d) ☒ No reply has been received.

2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
   (a) ☐ The issue fee and publication fee, if applicable, was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
   (b) ☐ The submitted fee of $_____ is insufficient. A balance of $_____ is due.
   The issue fee required by 37 CFR 1.18 is $_____. The publication fee, if required by 37 CFR 1.18(d), is $_____.
   (c) ☐ The issue fee and publication fee, if applicable, has not been received.

3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
   (a) ☐ Proposed corrected drawings were received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply.
   (b) ☐ No corrected drawings have been received.

4. ☐ The letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.

5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.

6. ☐ The decision by the Board of Patent Appeals and Interference rendered on _____ and because the period for seeking court review of the decision has expired and there are no allowed claims.

7. ☒ The reason(s) below:

See PTO-413.

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER

Phyllis G. Spivack
Primary Examiner
Art Unit: 1614

Petitions to revive under 37 CFR 1.137(a) or (b), or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.

Interview Summary	Application No.	Applicant(s)	
	09/895,141	BENZER ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Phyllis G. Spivack*. (3)_____.

(2) *Michael Rosato, RN 52,182*. (4)_____.

Date of Interview: _____.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____.

Claim(s) discussed: _____.

Identification of prior art discussed: _____.

Agreement with respect to the claims f)☒ was reached. g)☐ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Because the period for response ended on November 7, 2004, S.N. 09/895141 is abandoned*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

_____
Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.